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L3 ANSWER 1 OF 10 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
2003:462359 Document No.: PREV200300462359. Size exclusion chromatography as a tool for quality control of recombinant allergens and hypoallergenic variants. Weber, Bernhard [Reprint Author]; Slamal, Holger; Suck, Roland. Allergopharma Joachim Ganzer KG, Hermann-Koerner-Strasse 52, D-21465, Reinbek, Germany. bernhard.weber@allergopharma.de. Journal of Biochemical and Biophysical Methods, (30 June 2003) Vol. 56, No. 1-3, pp. 219-232. print.
ISSN: 0165-022X (ISSN print). Language: English.
AB Proteins or glycoproteins bearing epitopes for **human IgE antibodies** are designated as allergens causing type I allergic diseases. In this study, recombinant allergens were compared with their natural counterparts either as part of extracts or as purified molecules with respect to several biochemical and immunological properties. Natural and recombinant Bet v 1 and Phl p 1, major allergens of birch pollen extracts and Phleum pratense pollen extracts, were analyzed by SDS-PAGE,

immunoblotting, EAST inhibition and size exclusion chromatography (SEC). Differences of IgE-binding capacities between recombinant Bet v 1 as well as recombinant Phl p 1 variants were detected by EAST inhibition. These results were confirmed by size exclusion chromatography in that the recombinant proteins showed differences of their elution volumes being equivalent to the natural molecules only with the more active recombinant form. In contrast, SDS-PAGE and immunoblot analysis resulted in divergent characteristics, as either migrations of the variants were similar or no differences of IgE binding were detectable. In conclusion, size exclusion chromatography is the method of choice for quality control of well characterized recombinant allergens, comprising control of purity, protein content and conformation.

L3 ANSWER 2 OF 10 MEDLINE on STN DUPLICATE 1
2002451889 Document Number: 22197925. PubMed ID: 12209627. Conversion of grass pollen allergen-specific human IgE into a protective IgG(1) antibody. Flicker Sabine; Steinberger Peter; Norderhaug Lars; Sperr Wolfgang R; Majlesi Yasamin; Valent Peter; Kraft Dietrich; Valenta Rudolf. (Department of Pathophysiology, Vienna General Hospital, University of Vienna, Vienna, Austria.) EUROPEAN JOURNAL OF IMMUNOLOGY, (2002 Aug) 32 (8) 2156-62. Journal code: 1273201. ISSN: 0014-2980. Pub. country: Germany: Germany, Federal Republic of. Language: English.
AB More than 100 million individuals exhibit IgE-mediated allergic reactions against Phl p 2, a major allergen from **timothy grass** pollen. We isolated cDNA coding for three Phl p 2-specific **human IgE antibodies** from a combinatorial library, which was constructed from lymphocytes of a grass pollen-allergic patient. Recombinant Phl p 2-specific IgE antibody fragments (Fab) recognized a fragment comprising the 64 N-terminal amino acids of Phl p 2 and cross-reacted with group 2 allergens from seven grass species. cDNA coding for the variable regions of one of the IgE Fab were cloned into aplasmid vector expressing the constant region of human IgG(1) to obtain a complete, recombinant Phl p 2-specific human IgG(1). This antibody blocked the binding of grass pollen-allergic patients IgE (n=26; mean inhibition: 58%) to Phl p 2 and caused a 100-fold reduction of Phl p 2-induced basophil histamine release. The recombinant human Phl p 2-specific IgG(1) may be used for environmental allergen detection, for standardization of diagnostic as well as therapeutic grass pollen allergen preparations and for passive therapy of grass pollen allergy.

L3 ANSWER 3 OF 10 MEDLINE on STN DUPLICATE 2
2002489205 Document Number: 22209128. PubMed ID: 12220472. Molecular and immunological characterization of a novel **timothy grass** (Phleum pratense) pollen allergen, Phl p 11. Marknell DeWitt A; Niederberger V; Lehtonen P; Spitzauer S; Sperr W R; Valent P; Valenta R; Lidholm J. (Pharmacia Diagnostics AB, Uppsala, Sweden.) CLINICAL AND EXPERIMENTAL ALLERGY, (2002 Sep) 32 (9) 1329-40. Journal code: 8906443. ISSN: 0954-7894. Pub. country: England: United Kingdom. Language: English.
AB BACKGROUND: Allergy to grass pollen is typically associated with serum IgE antibodies to group 1 and/or group 5 allergens, and additionally often to one or several less prominent allergens. Most of the grass pollen allergens identified to date have been characterized in detail by molecular, biochemical and immunological methods, **timothy grass** being one of the most thoroughly studied species. However, a 20-kDa allergen frequently recognized by IgE antibodies from grass pollen allergics has so far escaped cloning and molecular characterization. OBJECTIVE: To clone and characterize the 20 kDa **timothy grass** pollen allergen Phl p 11. METHODS: Phl p 11 cDNA was cloned by PCR techniques, utilizing N-terminal amino acid sequence obtained from the natural allergen. Phl p 11 was expressed as a soluble fusion protein in Escherichia coli, purified to homogeneity and used for serological analysis and to study Phl p 11 specific induction of histamine release from basophils and skin reactivity in sensitized and control subjects. RESULTS: Phl p 11 cDNA defined an acidic polypeptide of 15.8 kDa with homology to pollen proteins from a variety of plant species

and to soybean trypsin inhibitor. The sequence contained one potential site for N-linked glycosylation. Serological analysis revealed that recombinant Phl p 11 shared epitopes for **human IgE antibodies** with the natural protein and bound serum IgE from 32% of grass pollen-sensitized subjects (n = 184). Purified recombinant Phl p 11 elicited skin reactions and dose-dependent histamine release from basophils of sensitized subjects, but not in non-allergic controls. CONCLUSION: As the first representative of group 11 grass pollen allergens, Phl p 11 has been cloned and produced as a recombinant protein showing allergenic activity. One-third of grass pollen-sensitized subjects showed specific IgE reactivity to recombinant Phl p 11, corresponding in magnitude to a significant proportion of specific IgE to grass pollen extract.

L3 ANSWER 4 OF 10 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

1998:667447 The Genuine Article (R) Number: 114KL. Molecular basis of IgE-recognition of Lol p 5, a major allergen of rye-grass pollen. Suphioglu C (Reprint); Blaher B; Rolland J M; McCluskey J; Schappi G; Kenrick J; Singh M B; Knox R B. ALFRED HOSP, MONASH MED SCH, DEPT ALLERGY & CLIN IMMUNOL, PRAHRAN, VIC 3052, AUSTRALIA (Reprint); UNIV MELBOURNE, SCH BOT, POLLEN & ALLERGEN RES GRP, PARKVILLE, VIC 3052, AUSTRALIA; MONASH UNIV, DEPT PATHOL & IMMUNOL, PRAHRAN, VIC 3181, AUSTRALIA; UNIV MELBOURNE, DEPT MICROBIOL & IMMUNOL, PARKVILLE, VIC 3052, AUSTRALIA; UNIV MELBOURNE, DEPT AGR & RESOURCE MANAGEMENT, PARKVILLE, VIC 3052, AUSTRALIA. MOLECULAR IMMUNOLOGY (APR 1998) Vol. 35, No. 5, pp. 293-305. Publisher: PERGAMON-ELSEVIER SCIENCE LTD. THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND. ISSN: 0161-5890. Pub. country: AUSTRALIA. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Grass pollen, especially of lye-grass (Lolium perenne), represents an important cause of type I allergy. Identification of IgE-binding (allergenic) epitopes of major grass pollen allergens is essential for understanding the molecular basis of interaction between allergens and **human IgE antibodies** and therefore facilitates the devising of safer and more effective diagnostic and immunotherapy reagents. The aim of this study was to identify the allergenic epitopes of Lol p 5, a major allergen of rye-grass pollen, immunodissect these epitopes further so that the amino acid residues critical for antibody binding can be determined and investigate the conservation and nature of these epitopes within the context of the natural grass pollen allergens. Peptides, 12-13 amino acid residues long and overlapping each other by 3 amino acid residues, based on the entire deduced amino acid sequence of the coding region of Lol p 5, were synthesised and assayed for IgE-binding. Two strong IgE-binding epitopes (Lol p 5 (49-60) and (265-276), referred to as peptides 7 and 34, respectively) were identified. These epitopes were further resolved by truncated peptides and amino acid replacement studies and the amino acid residues critical for IgE-binding determined (Lol p 5 (49-60) residue Lys,, and (265-276) residue Lys,,,). Sequences of these epitopes were conserved in related allergens and may form the conserved allergenic domains responsible for the cross-reactivity observed between pollen allergens of taxonomically related grasses. Furthermore, due to its strong IgE-reactivity, synthetic peptide Lol p 5 (265-276) was used to affinity-purify specific IgE antibodies which recognised proteins of other clinically important grass pollens, further indicating presence of allergenic cross-reactivity at the level of allergenic epitope. Moreover, Lol p 5 (265-276) demonstrated a strong capacity to inhibit IgE-binding to natural rye-grass pollen proteins highlighting the antibody accessibility to these sequences within the context of the natural allergens. Strong IgE-binding epitopes of Lol p 5 have been identified down to single critical amino acid residues and are shown to occur as linear or continuous domains in the natural conformation of natural Lol p 5 and other group 5 grass pollen allergens. The fact that such an allergenic synthetic epitope has the capacity to strongly inhibit IgE-binding to natural allergens highlight its potential for use as a candidate in future therapeutics to treat pollen-associated allergies. (C)

L3 ANSWER 5 OF 10 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
1998:380416 Document No.: PREV199800380416. Isolation and characterization of recombinant **human IgE antibody** fragments (Fabs) with specificity for the major **timothy grass** pollen allergen Phl p 2. Flicker, Sabine; Steinberger, Peter; Dolecek, Christiane; Kraft, Dietrich; Valenta, Rudolf. Inst. General and Experimental Pathol., AKH, Univ. Vienna, Vienna, Austria. Allergy (Copenhagen), (1998) Vol. 53, No. SUPPL. 43, pp. 113. print.
Meeting Info.: Annual Meeting of the European Academy of Allergology and Clinical Immunology. Birmingham, England, UK. June 21-26, 1998. European Academy of Allergology and Clinical Immunology.
CODEN: LLRGDY. ISSN: 0105-4538. Language: English.

L3 ANSWER 6 OF 10 MEDLINE on STN DUPLICATE 3
97276847 Document Number: 97276847. PubMed ID: 9130540. Expression in Escherichia coli of **human IgE antibody** fragments with specificity for major **timothy grass** pollen allergens using the combinatorial library approach. Steinberger P; Kraft D; Valenta R. (Institute of General and Experimental Pathology, AKH, University of Vienna, Austria.) INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (1997 May-Jul) 113 (1-3) 258-9. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

L3 ANSWER 7 OF 10 MEDLINE on STN DUPLICATE 4
96210038 Document Number: 96210038. PubMed ID: 8631916. Construction of a combinatorial IgE library from an allergic patient. Isolation and characterization of human IgE Fabs with specificity for the major **timothy grass** pollen allergen, Phl p 5. Steinberger P; Kraft D; Valenta R. (Institute of General and Experimental Pathology, AKH, University of Vienna, Austria.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 May 3) 271 (18) 10967-72. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.
AB To characterize **human IgE antibodies** with specificity for a major allergen at the molecular level, we have constructed an IgE combinatorial library from a grass pollen allergic patient. cDNAs coding for IgE heavy chain fragments and for light chains were reverse-transcribed and polymerase chain reaction-amplified from RNA of peripheral blood lymphocytes and randomly combined in plasmid pComb3H to yield a combinatorial library of 5 x 10(7) primary clones. IgE Fabs with specificity for Phl p 5, a major **timothy grass** pollen allergen, were isolated by panning. Sequence analysis showed that the 4 of the Fabs used the same heavy chain fragments which had combined with different kappa light chains. Soluble recombinant IgE Fabs were purified by affinity chromatography to Phl p 5 and, like natural IgE antibodies, cross-reacted with group 5 allergens from different grass species. The described approach should facilitate studies on the molecular interaction between IgE antibodies and allergens and encourages the consideration of specific IgE Fabs that are capable of interfering with allergen-IgE binding as potential therapeutic tools.

L3 ANSWER 8 OF 10 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
1995:383362 Document No.: PREV199598397662. Cloning and expression of functional **human IgE-antibody**-fragments specific for a major **Timothy grass** pollen allergen (Phl p5). Steinberger, P.; Kraft, D.; Valenta, R.. Inst. Gen. Exp. Pathol., Vienna, Austria. 9TH INTERNATIONAL CONGRESS OF IMMUNOLOGY. (1995) pp. 466. The 9th International Congress of Immunology. Publisher: 9th International Congress of Immunology, San Francisco, California, USA.
Meeting Info.: Meeting Sponsored by the American Association of Immunologists and the International Union of Immunological Societies. San Francisco, California, USA. July 23-29, 1995.
Language: English.

L3 ANSWER 9 OF 10 MEDLINE on STN DUPLICATE 5
95375563 Document Number: 95375563. PubMed ID: 7544180. Characterization of the allergen group VI in **timothy grass** pollen (Phl p 6). I. Immunological and biochemical studies. Petersen A; Bufe A; Schlaak M; Becker W M. (Division of Allergology, Forschungsinstitut Borstel, Germany.) INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (1995 Sep) 108 (1) 49-54. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB For the identification and characterization of allergen grass group VI we performed two-dimensional immunoblotting of **timothy grass** pollen (Phleum pratense). Two intense 13-kD protein spots of pI 5.2 and 5.5 were found to be IgE reactive. By N-terminal microsequencing and amino acid analysis we identified them as Phl p 6 isoallergens. An antiserum was raised against Phl p 6 by immunizing BALB/c mice with allergen bearing nitrocellulose particles of one isoform. The antiserum revealed an intense reactivity to Phl p 6 isoforms, but also showed a weak cross-reactivity with Phl p 5 allergens. After immunoabsorption of patients' serum to Phl p 6 spots on the blotting membrane, we were able to demonstrate that the eluted **human IgE antibodies** cross-react with the grass group V allergens as well. Therefore, Phl p 5 and Phl p 6 possess one or more common IgE binding epitopes.

L3 ANSWER 10 OF 10 MEDLINE on STN DUPLICATE 6
77206353 Document Number: 77206353. PubMed ID: 406207. Chemical modification of crude **timothy grass** pollen extract. III. The effect of glutaraldehyde-induced aggregation on antigenic and immunogenic properties. Moran D M; Wheeler A W; Overell B G; Woroniecki S R. INTERNATIONAL ARCHIVES OF ALLERGY AND APPLIED IMMUNOLOGY, (1977) 54 (4) 315-21. Journal code: 0404561. ISSN: 0020-5915. Pub. country: Switzerland. Language: English.

AB Timothy pollen extracts have been reacted with glutaraldehyde under conditions leading to different degrees of aggregation of the product. Aggregation tends to enhance the previously demonstrated effects of glutaraldehyde in that reactivity with **human IgE antibody**, and ability to induce IgE antibody in the Bordetella pertussis-treated rat, are further reduced. Ability to induce IgG antibody with specificity for unmodified extract is substantially retained in all aggregated products.

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L4 24 HUMAN IGE FAB

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L5 9 DUP REMOVE L4 (15 DUPLICATES REMOVED)

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L5 ANSWER 1 OF 9 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 1
2001:202317 Document No.: PREV200100202317. Construction and characterization of **human IgE Fab** fragments specific to peanut allergens. Ling, Min [Reprint author]; Sen, Moon [Reprint author]; West, Charles M. [Reprint author]; Sampson, Hugh A.; Burks, A. W. [Reprint author]; Bannon, Gary A. [Reprint author]. University of Arkansas for Medical Sciences, Little Rock, AR, USA. Journal of Allergy and Clinical Immunology, (February, 2001) Vol. 107, No. 2, pp. S290-S291. print. Meeting Info.: 57th Annual Meeting of the American Academy of Allergy, Asthma and Immunology. New Orleans, Louisiana, USA. March 16-21, 2001. American Academy of Allergy Asthma and Immunology. CODEN: JACIBY. ISSN: 0091-6749. Language: English.

L5 ANSWER 2 OF 9 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

2001:178135 Document No.: PREV200100178135. Recombinant **human IgE-Fabs** with specificity for group 2 grass pollen allergens for prevention, diagnosis and therapy of grass pollen allergy. Flicker, Sabine [Reprint author]; Steinberger, Peter [Reprint author]; Kraft, Dietrich [Reprint author]; Valenta, Rudolf [Reprint author]. Molecular Immunpathology, Vienna, Austria. Journal of Allergy and Clinical Immunology, (February, 2001) Vol. 107, No. 2, pp. S179. print. Meeting Info.: 57th Annual Meeting of the American Academy of Allergy, Asthma and Immunology. New Orleans, Louisiana, USA. March 16-21, 2001. American Academy of Allergy Asthma and Immunology. CODEN: JACIBY. ISSN: 0091-6749. Language: English.

L5 ANSWER 3 OF 9 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
2001:200643 The Genuine Article (R) Number: 405RE. Recombinant **human IgE-Fabs** with specificity for group 2 grass pollen allergens for prevention, diagnosis and therapy of grass pollen allergy. Flicker S (Reprint); Steinberger P; Kraft D; Valenta R. JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY (FEB 2001) Vol. 107, No. 2, Supp. [S], pp. S179-S179. MA 588. Publisher: MOSBY, INC. 11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO 63146-3318 USA. ISSN: 0091-6749. Language: English.

L5 ANSWER 4 OF 9 MEDLINE on STN DUPLICATE 2
2000485731 Document Number: 20487204. PubMed ID: 11034391. A human monoclonal IgE antibody defines a highly allergenic fragment of the major timothy grass pollen allergen, Phl p 5: molecular, immunological, and structural characterization of the epitope-containing domain. Flicker S; Vrtala S; Steinberger P; Vangelista L; Bufe A; Petersen A; Ghannadan M; Sperr W R; Valent P; Norderhaug L; Bohle B; Stockinger H; Suphioglu C; Ong E K; Kraft D; Valenta R. (Department of Pathophysiology, University of Vienna, Austria.) JOURNAL OF IMMUNOLOGY, (2000 Oct 1) 165 (7) 3849-59. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.
AB Almost 90% of grass pollen-allergic patients are sensitized against group 5 grass pollen allergens. We isolated a monoclonal **human IgE Fab** out of a combinatorial library prepared from lymphocytes of a grass pollen-allergic patient and studied its interaction with group 5 allergens. The IgE Fab cross-reacted with group 5A isoallergens from several grass and corn species. By allergen gene fragmentation we mapped the binding site of the IgE Fab to a 11.2-kDa N-terminal fragment of the major timothy grass pollen allergen Phl p 5A. The IgE Fab-defined Phl p 5A fragment was expressed in Escherichia coli and purified to homogeneity. Circular dichroism analysis revealed that the rPhl p 5A domain, as well as complete rPhl p 5A, assumed a folded conformation consisting predominantly of an alpha helical secondary structure, and exhibited a remarkable refolding capacity. It reacted with serum IgE from 76% of grass pollen-allergic patients and revealed an extremely high allergenic activity in basophil histamine release as well as skin test experiments. Thus, the rPhl p 5A domain represents an important allergen domain containing several IgE epitopes in a configuration optimal for efficient effector cell activation. We suggest the rPhl p 5A fragment and the corresponding IgE Fab as paradigmatic tools to explore the structural requirements for highly efficient effector cell activation and, perhaps later, for the development of generally applicable allergen-specific therapy strategies.

L5 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
1997:282896 Document No. 126:329233 Expression in Escherichia coli of human IgE antibody fragments with specificity for major timothy grass pollen allergens using the combinatorial library approach. Steinberger, Peter; Kraft, Dietrich; Valenta, Rudolf (Institute of General and Experimental Pathology, AKH, University of Vienna, Vienna, A-1090, Austria). International Archives of Allergy and Immunology, 113(1-3), 258-259 (English) 1997. CODEN: IAAIEG. ISSN: 1018-2438. Publisher: Karger.
AB An IgE combinatorial library was constructed from a patient who was allergic to grass pollen. Recombinant **human IgE**

Fab fragments with specificity for major grass pollen allergens were isolated.

L5 ANSWER 6 OF 9 MEDLINE on STN DUPLICATE 3
96210038 Document Number: 96210038. PubMed ID: 8631916. Construction of a combinatorial IgE library from an allergic patient. Isolation and characterization of **human IgE Fabs** with specificity for the major timothy grass pollen allergen, Phl p 5. Steinberger P; Kraft D; Valenta R. (Institute of General and Experimental Pathology, AKH, University of Vienna, Austria.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 May 3) 271 (18) 10967-72. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB To characterize human IgE antibodies with specificity for a major allergen at the molecular level, we have constructed an IgE combinatorial library from a grass pollen allergic patient. cDNAs coding for IgE heavy chain fragments and for light chains were reverse-transcribed and polymerase chain reaction-amplified from RNA of peripheral blood lymphocytes and randomly combined in plasmid pComb3H to yield a combinatorial library of 5 x 10(7) primary clones. IgE Fabs with specificity for Phl p 5, a major timothy grass pollen allergen, were isolated by panning. Sequence analysis showed that the 4 of the Fabs used the same heavy chain fragments which had combined with different kappa light chains. Soluble recombinant IgE Fabs were purified by affinity chromatography to Phl p 5 and, like natural IgE antibodies, cross-reacted with group 5 allergens from different grass species. The described approach should facilitate studies on the molecular interaction between IgE antibodies and allergens and encourages the consideration of specific IgE Fabs that are capable of interfering with allergen-IgE binding as potential therapeutic tools.

L5 ANSWER 7 OF 9 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
94:713888 The Genuine Article (R) Number: PQ006. GLYCATION OF MONOCLONAL-ANTIBODIES IMPAIRS THEIR ABILITY TO BIND ANTIGEN. KENNEDY D M (Reprint); SKILLEN A W; SELF C H. CITY HOSP NOTTINGHAM, DEPT CLIN CHEM, HUCKNALL RD, NOTTINGHAM NG5 1PB, ENGLAND (Reprint); UNIV NEWCASTLE UPON TYNE, DEPT CLIN BIOCHEM, NEWCASTLE UPON TYNE, TYNE & WEAR, ENGLAND. CLINICAL AND EXPERIMENTAL IMMUNOLOGY (NOV 1994) Vol. 98, No. 2, pp. 245-251. ISSN: 0009-9104. Pub. country: ENGLAND. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB As elevated levels of glycated IgG have been detected in the plasma of patients with diabetes mellitus, a disease associated with increased susceptibility to infection, we have investigated whether glycation of MoAbs affects the kinetics and/or affinity of antigen binding. Three mouse MoAbs were incubated with 0.5 M glucose at pH 7.4 for 14-21 days at 37 degrees C. Control MoAbs were incubated using identical conditions but with no added glucose. Using a surface plasmon resonance technique we found that glycation significantly increased the rate of dissociation (k(diss)) of the antigen-antibody complex for all three MoAbs ($P < 0.05$, $n = 4$), but had no significant effect on the rate of association (k(ass)). For one of the MoAbs, against **human Ige** (**Fab**), we also measured k(diss) by an alternative method utilizing radiolabelled antigen, which confirmed that glycation of the antibody significantly increases k(diss) ($P < 0.001$, $n = 8$). We also found using an ELISA-based method that glycation of the same MoAb significantly increased the equilibrium dissociation constant (K-d) ($P < 0.05$, $n = 6$) A significant increase in k(d) was observed after glycation using glucose concentrations consistent with those found in poorly controlled diabetics ($P < 0.02$, $n = 5$). We conclude that in vitro glycation can significantly lower the affinity of an antibody for its antigen, and significantly increases the rate of dissociation of the antigen-antibody complex.

L5 ANSWER 8 OF 9 MEDLINE on STN DUPLICATE 4
92259988 Document Number: 92259988. PubMed ID: 1583314. Isolation and amplification of human IgE Fd encoding mRNA from human peripheral blood lymphocytes. Walker M R; Bevan L J; Daniels J; Rottier M M; Rapley R; Roberts A M. (Molecular Biology Research Group, University Department of

Clinical Biochemistry, Wolfson Research Laboratories, Queen Elizabeth Medical Centre, Edgbaston, Birmingham, UK.) JOURNAL OF IMMUNOLOGICAL METHODS, (1992 Apr 27) 149 (1) 77-85. Journal code: 1305440. ISSN: 0022-1759. Pub. country: Netherlands. Language: English.

AB In order to establish the feasibility of applying recombinatorial library technologies to investigate human in vivo IgE responses, and as a pre-requisite of recombinatorial library construction, we have attempted to determine workable peripheral blood sample volumes required for isolation of mRNA for polymerase chain reaction (PCR) amplification of human IgE Fd encoding sequences. Cells secreting chimeric human IgE monoclonal antibody specific for the hapten NIP were used to establish the conditions for specific amplification of C epsilon 1 domain and Fd encoding sequences, as determined by Southern hybridisation. Amplification of C epsilon 1 domain sequences could be achieved using as few as ten cultured cells as the source of RNA. Specific IgE+ B cell enrichment using immuno-magnetic particles prior to RNA extraction was, however, required to obtain amplification of IgE C epsilon 1 and Fd fragments from lymphocytes prepared from 40 ml human peripheral blood. IgG1+ B cell enrichment from similar samples was not required for detectable amplification of human C gamma 1 cDNA sequences. However, this procedure improved amplification efficiency. Optimisation of methods to separate specific B cell populations, or specific RNA/cDNA sequences, will facilitate in vitro generation of **human IgE** **Fab** fragments from peripheral blood.

L5 ANSWER 9 OF 9 MEDLINE on STN DUPLICATE 5

82070764 Document Number: 82070764. PubMed ID: 6796293. Highly sensitive sandwich enzyme immunoassay of human IgE with beta-D-galactosidase from Escherichia coli. Imagawa M; Yoshitake S; Ishikawa E; Endo Y; Ohtaki S; Kano E; Tsunetoshi Y. CLINICA CHIMICA ACTA, (1981 Dec 9) 117 (2) 199-207. Journal code: 1302422. ISSN: 0009-8981. Pub. country: Netherlands. Language: English.

AB A highly sensitive sandwich enzyme immunoassay of human IgE was developed. Polystyrene balls were coated with goat anti-human IgE immunoglobulin (IgG) by physical adsorption. Goat anti-**human IgE** **Fab**' was purified by affinity chromatography and conjugated with beta-D-galactosidase from Escherichia coli. Using thus prepared anti-IgE-coated polystyrene balls and anti-IgE-beta-D-galactosidase conjugate, 0.2 mU (2 amol)--1 U of IgE per assay could be determined. When 0.1 microliter of serum per assay was used, the range of IgE levels in serum that could be determined was 2--10000 U/ml, and even 0.01 U/ml was measurable by using 20 microliters of serum. The regression equation and coefficient for correlation to radioimmunoassay were gamma (RIA) = 0.94 chi (EIA) + 18.2 and 0.96 (n = 81), respectively. The coefficients of within- and between-assay variations ranged from 5.4 to 8.5%. The mean levels of serum IgE determined by the present assay were 103 U/ml in 70 normal children and 1064 U/ml in 38 children with bronchial asthma.

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=> s (flicker s?/au or steinberger p?/au or kraft d?/au or valenta r?/au)
L6        2901 (FLICKER S?/AU OR STEINBERGER P?/AU OR KRAFT D?/AU OR VALENTA
               R?/AU)

=> s l6 and Fab library
L7           0 L6 AND FAB LIBRARY

=> s l6 and IgE Fab
L8          27 L6 AND IGE FAB

=> dup remove l8
PROCESSING COMPLETED FOR L8
L9           11 DUP REMOVE L8 (16 DUPLICATES REMOVED)

=> d l9 1-11 cbib abs
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L9 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
2002:777988 Document No. 137:277815 Novel compound for treatment of allergy and asthma. Laffer, Sylvia; Roux, Kenneth H.; Sperr, Wolfgang R.; Valent, Peter; **Kraft, Dietrich**; **Valenta, Rudolf**; Hoegbom, Erik; Adriansson, Jonas; Groenlund, Hans (Pharmacia Diagnostics AB, Swed.). PCT Int. Appl. WO 2002079257 A1 20021010, 28 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-SE636 20020328. PRIORITY: SE 2001-1093 20010328.

AB The present invention relates to a novel drug candidate having a potential for universal therapy of allergy and asthma. The invention provides an anti-**IgE Fab** (antibody fragment) of IgG1 isotype, having the following characteristics: (a) inhibits the IgE-FcεRI interaction; (b) binds to free and cell-bound IgE; and (c) is non-anaphylactic.

L9 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
2002:521791 Document No. 137:77888 Timothy grass allergen-specific **IgE Fab** fragments and Fab-grafted IgG: diagnosis and therapy of type I allergy. **Flicker, Sabine**; **Steinberger, Peter**; **Kraft, Dietrich**; **Valenta, Rudolf** (Pharmacia Diagnostics AB, Swed.). PCT Int. Appl. WO 2002053595 A1 20020711, 45 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-SE2908 20011227. PRIORITY: SE 2000-4892 20001229.

AB The authors disclose the sequence characterization and grass/corn pollen cross-reactivity of human Fab fragments derived from IgE specific for Phl p2 allergen.

L9 ANSWER 3 OF 11 MEDLINE on STN DUPLICATE 1
2002451889 Document Number: 22197925. PubMed ID: 12209627. Conversion of grass pollen allergen-specific human IgE into a protective IgG(1) antibody. **Flicker Sabine**; **Steinberger Peter**; Norderhaug Lars; Sperr Wolfgang R; Majlesi Yasamin; Valent Peter; **Kraft Dietrich**; **Valenta Rudolf.** (Department of Pathophysiology, Vienna General Hospital, University of Vienna, Vienna, Austria.) EUROPEAN JOURNAL OF IMMUNOLOGY, (2002 Aug) 32 (8) 2156-62. Journal code: 1273201. ISSN: 0014-2980. Pub. country: Germany: Germany, Federal Republic of. Language: English.

AB More than 100 million individuals exhibit IgE-mediated allergic reactions against Phl p 2, a major allergen from timothy grass pollen. We isolated cDNA coding for three Phl p 2-specific human IgE antibodies from a combinatorial library, which was constructed from lymphocytes of a grass pollen-allergic patient. Recombinant Phl p 2-specific IgE antibody fragments (Fab) recognized a fragment comprising the 64 N-terminal amino acids of Phl p 2 and cross-reacted with group 2 allergens from seven grass species. cDNA coding for the variable regions of one of the **IgE Fab** were cloned into aplasmid vector expressing the constant region of human IgG(1) to obtain a complete, recombinant Phl p 2-specific human IgG(1). This antibody blocked the binding of grass pollen-allergic patients IgE (n=26; mean inhibition: 58%) to Phl p 2 and caused a 100-fold reduction of Phl p 2-induced basophil histamine release. The recombinant

human Phl p 2-specific IgG(1) may be used for environmental allergen detection, for standardization of diagnostic as well as therapeutic grass pollen allergen preparations and for passive therapy of grass pollen allergy.

L9 ANSWER 4 OF 11 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
2001:178135 Document No.: PREV200100178135. Recombinant human **IgE-Fabs** with specificity for group 2 grass pollen allergens for prevention, diagnosis and therapy of grass pollen allergy. **Flicker, Sabine** [Reprint author]; **Steinberger, Peter** [Reprint author]; **Kraft, Dietrich** [Reprint author]; **Valenta, Rudolf** [Reprint author]. Molecular Immunpathology, Vienna, Austria. Journal of Allergy and Clinical Immunology, (February, 2001) Vol. 107, No. 2, pp. S179. print.
Meeting Info.: 57th Annual Meeting of the American Academy of Allergy, Asthma and Immunology. New Orleans, Louisiana, USA. March 16-21, 2001. American Academy of Allergy Asthma and Immunology.
CODEN: JACIBY. ISSN: 0091-6749. Language: English.

L9 ANSWER 5 OF 11 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
2001:200643 The Genuine Article (R) Number: 405RE. Recombinant human **IgE-Fabs** with specificity for group 2 grass pollen allergens for prevention, diagnosis and therapy of grass pollen allergy.
Flicker S (Reprint); Steinberger P; Kraft D; Valenta R. JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY (FEB 2001) Vol. 107, No. 2, Supp. [S], pp. S179-S179. MA 588. Publisher: MOSBY, INC. 11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO 63146-3318 USA. ISSN: 0091-6749 . Language: English.

L9 ANSWER 6 OF 11 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 2
2001145732 EMBASE A highly allergenic fragment of the major timothy grass pollen allergen, Phl p 5, defined by a human monoclonal IgE antibody.
Flicker S.; Vrtala S.; **Steinberger P.**; Vangelista L.; **Kraft D.**; **Valenta R.**. Dr. R. Valenta, Department of Pathophysiology, AKH, University of Vienna, Wahringer Gurtel 18-20, A-1090 Vienna, Austria. Rudolf.Valenta@akh-wien.ac.at. International Archives of Allergy and Immunology 124/1-3 (80-84) 2001.
Refs: 16.
ISSN: 1018-2438. CODEN: IAAIEG. Pub. Country: Switzerland. Language: English. Summary Language: English.
AB We report the characterization of a domain of the major timothy grass pollen allergen, Phl p 5A, which contains the binding site for a human monoclonal IgE antibody. The human monoclonal IgE antibody fragment (Fab) was obtained from an IgE combinatorial library constructed from lymphocytes of a grass pollen-allergic patient. An 11.2-kD N-terminal fragment representing approximately one third of the complete Phl p 5A allergen could be identified to contain the binding site for the **IgE Fab.** The rPhl p 5A fragment revealed an extremely high allergenic activity in skin test experiments which in some cases equaled that of the complete Phl p 5A allergen. The rPhl p 5A domain thus represents an allergen fragment containing several IgE epitopes in a configuration optimal for efficient effector cell activation. We suggest the rPhl p 5A fragment and the corresponding **IgE Fab** as paradigmatic tools to explore the structural requirements for highly efficient effector cell activation. Copyright .COPYRGT. 2001 S. Karger AG, Basel.

L9 ANSWER 7 OF 11 MEDLINE on STN DUPLICATE 3
2000485731 Document Number: 20487204. PubMed ID: 11034391. A human monoclonal IgE antibody defines a highly allergenic fragment of the major timothy grass pollen allergen, Phl p 5: molecular, immunological, and structural characterization of the epitope-containing domain. **Flicker S**; Vrtala S; **Steinberger P**; Vangelista L; Bufe A; Petersen A; Ghannadan M; Sperr W R; Valent P; Norderhaug L; Bohle B; Stockinger H;

Suphioglu C; Ong E K; **Kraft D**; **Valenta R.** (Department of Pathophysiology, University of Vienna, Austria.) JOURNAL OF IMMUNOLOGY, (2000 Oct 1) 165 (7) 3849-59. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Almost 90% of grass pollen-allergic patients are sensitized against group 5 grass pollen allergens. We isolated a monoclonal human **IgE Fab** out of a combinatorial library prepared from lymphocytes of a grass pollen-allergic patient and studied its interaction with group 5 allergens. The **IgE Fab** cross-reacted with group 5A isoallergens from several grass and corn species. By allergen gene fragmentation we mapped the binding site of the **IgE Fab** to a 11.2-kDa N-terminal fragment of the major timothy grass pollen allergen Phl p 5A. The **IgE Fab**-defined Phl p 5A fragment was expressed in Escherichia coli and purified to homogeneity. Circular dichroism analysis revealed that the rPhl p 5A domain, as well as complete rPhl p 5A, assumed a folded conformation consisting predominantly of an alpha helical secondary structure, and exhibited a remarkable refolding capacity. It reacted with serum IgE from 76% of grass pollen-allergic patients and revealed an extremely high allergenic activity in basophil histamine release as well as skin test experiments. Thus, the rPhl p 5A domain represents an important allergen domain containing several IgE epitopes in a configuration optimal for efficient effector cell activation. We suggest the rPhl p 5A fragment and the corresponding **IgE Fab** as paradigmatic tools to explore the structural requirements for highly efficient effector cell activation and, perhaps later, for the development of generally applicable allergen-specific therapy strategies.

L9 ANSWER 8 OF 11 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN DUPLICATE 4

97:335059 The Genuine Article (R) Number: WV647. Expression in Escherichia coli of human IgE antibody fragments with specificity for major timothy grass pollen allergens using the combinatorial library approach. **Steinberger P; Kraft D; Valenta R (Reprint).** UNIV VIENNA, INST GEN & EXPT PATHOL, AKH, WUHRINGER GURTEL 18-20, A-1090 VIENNA, AUSTRIA (Reprint); UNIV VIENNA, INST GEN & EXPT PATHOL, AKH, A-1090 VIENNA, AUSTRIA. INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY (MAY 1997) Vol. 113, No. 1-3, pp. 258-259. Publisher: KARGER. ALLSCHWILERS TRASSE 10, CH-4009 BASEL, SWITZERLAND. ISSN: 1018-2438. Pub. country: AUSTRIA. Language: English.

L9 ANSWER 9 OF 11 MEDLINE on STN DUPLICATE 5

1998045195 Document Number: 98045195. PubMed ID: 9383913. Cloning allergen-specific antibody fragments (Fabs); tools for allergen standardization and therapy of type I allergy. **Valenta R**; **Steinberger P**; Laffer S; Dolecek C; Wiedemann P; **Flicker S** ; **Kraft D.** ARBEITEN AUS DEM PAUL-EHRLICH-INSTITUT (BUNDESAMT FUR SERA UND IMPFSTOFFE) ZU FRANKFURT A.M., (1997) (91) 222-9. Ref: 31. Journal code: 8912864. ISSN: 0936-8671. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.

AB Recombinant allergens have made it possible to dissect the mechanisms of allergen-antibody interactions at a molecular level. It becomes clear that monoclonal human IgG antibodies as well as animal derived antibodies can block the interaction of specific IgE antibodies as well as the allergen induced allergic effector reaction. Using PCR technology and combinatorial plasmid vectors, recombinant antibody fragments can be produced and it has even become possible to isolate allergen-specific **IgE Fabs** out of combinatorial IgE libraries constructed from allergic patients lymphocytes. Recombinant Fabs will represent useful tools to study the IgE-allergen interaction as well as for the standardization of allergen extracts and quantitative allergen measurements. Moreover, allergen-specific recombinant Fabs which block the allergen-IgE interaction have to be considered as tools for local therapy in effector organs of allergic patients.

L9 ANSWER 10 OF 11 MEDLINE on STN DUPLICATE 6

96210038 Document Number: 96210038. PubMed ID: 8631916. Construction of a combinatorial IgE library from an allergic patient. Isolation and characterization of human **IgE Fabs** with specificity for the major timothy grass pollen allergen, Phl p 5. **Steinberger P; Kraft D; Valenta R.** (Institute of General and Experimental Pathology, AKH, University of Vienna, Austria.) JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 May 3) 271 (18) 10967-72. Journal code: 2985121R. ISSN: 0021-9258. Pub. country: United States. Language: English.

AB To characterize human IgE antibodies with specificity for a major allergen at the molecular level, we have constructed an IgE combinatorial library from a grass pollen allergic patient. cDNAs coding for IgE heavy chain fragments and for light chains were reverse-transcribed and polymerase chain reaction-amplified from RNA of peripheral blood lymphocytes and randomly combined in plasmid pComb3H to yield a combinatorial library of 5 x 10(7) primary clones. **IgE Fabs** with specificity for Phl p 5, a major timothy grass pollen allergen, were isolated by panning. Sequence analysis showed that the 4 of the Fabs used the same heavy chain fragments which had combined with different kappa light chains. Soluble recombinant **IgE Fabs** were purified by affinity chromatography to Phl p 5 and, like natural IgE antibodies, cross-reacted with group 5 allergens from different grass species. The described approach should facilitate studies on the molecular interaction between IgE antibodies and allergens and encourages the consideration of specific **IgE Fabs** that are capable of interfering with allergen-IgE binding as potential therapeutic tools.

L9 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

1993:647466 Document No. 119:247466 Recombinant allergens as candidates for immunotherapy of type I allergic diseases. **Valenta, Rudolf;** Duchene, Michael; Vrtala, Susanne; Ball, Tanja; Ferreira, Fatima; Laffer, Sylvia; Hirschwehr, Reinhold; Ebner, Christof; Sperr, Wolfgang; et al. (Inst. Gen. Exp. Pathol., Univ. Vienna, Vienna, A-1090, Austria). Vaccines 93, [Annu. Meet.], 10th, Meeting Date 1992, 37-42. Editor(s): Ginsberg, Harold S. Cold Spring Harbor Lab.: Cold Spring Harbor, N. Y. (English) 1993. CODEN: 59HUAJ.

AB Based on the possibility of defining a limited panel of relevant recombinant tree and grass pollen allergens (Bet v I, profilin, Phi p I, and Phl p V), patient-tailored immunotherapy appears to be a realistic approach for the management of allergic diseases. Allergy vaccination could comprise active immunotherapy with recombinant allergens aimed at switching from Th2 to Th1 responses, the use of peptides containing IgE haptens, or allergen-specific **IgE Fabs.**

```
=> s IgE Fab
L10         83 IGE FAB

=> s l10 and grafting
L11          0 L10 AND GRAFTING

=> s l10 and IgE-Fd
L12          5 L10 AND IGE-FD

=> s l12 and "Phl p2"
L13          0 L12 AND "PHL P2"

=> s l10 and "phl p2"
L14          1 L10 AND "PHL P2"

=> d l14 cbib abs
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L14 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN

2002:521791 Document No. 137:77888 Timothy grass allergen-specific **IgE Fab** fragments and Fab-grafted IgG: diagnosis and therapy of type I allergy. Flicker, Sabine; Steinberger, Peter; Kraft,

Dietrich; Valenta, Rudolf (Pharmacia Diagnostics AB, Swed.). PCT Int. Appl. WO 2002053595 A1 20020711, 45 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-SE2908 20011227. PRIORITY: SE 2000-4892 20001229.

AB The authors disclose the sequence characterization and grass/corn pollen cross-reactivity of human Fab fragments derived from IgE specific for **Phl p2** allergen.

=> s Phl p2 IgE antibody
L15 0 PHL P2 IGE ANTIBODY

=> s phl p2
L16 8 PHL P2

=> dup remove l16
PROCESSING COMPLETED FOR L16
L17 6 DUP REMOVE L16 (2 DUPLICATES REMOVED)

=> d l17 1-6 cbib abs

L17 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

2002:521791 Document No. 137:77888 Timothy grass allergen-specific IgE Fab fragments and Fab-grafted IgG: diagnosis and therapy of type I allergy. Flicker, Sabine; Steinberger, Peter; Kraft, Dietrich; Valenta, Rudolf (Pharmacia Diagnostics AB, Swed.). PCT Int. Appl. WO 2002053595 A1 20020711, 45 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-SE2908 20011227. PRIORITY: SE 2000-4892 20001229.

AB The authors disclose the sequence characterization and grass/corn pollen cross-reactivity of human Fab fragments derived from IgE specific for **Phl p2** allergen.

L17 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

2001:811046 Document No. 136:101009 Skin test results but not serology reflect immediate type respiratory sensitivity: a study performed with recombinant allergen molecules. Niederberger, Verena; Stubner, Petra; Spitzauer, Susanne; Kraft, Dietrich; Valenta, Rudolf; Ehrenberger, Klaus; Horak, Friedrich (Department of Otorhinolaryngology, Institute of Medical and Chemical Laboratory Diagnostics AKH, University of Vienna, Vienna, A-1090, Austria). Journal of Investigative Dermatology, 117(4), 848-851 (English) 2001. CODEN: JIDEAE. ISSN: 0022-202X. Publisher: Blackwell Science, Inc..

AB The diagnosis of type I allergy, an IgE-antibody-mediated hypersensitivity disease affecting more than 25% of the population, is based on the measurement of allergen-specific serum IgE levels and provocation testing. Whether the determination of allergen-specific serum IgE levels can replace in vivo provocation testing for allergy diagnosis is a controversial issue. We used purified recombinant timothy grass and birch pollen allergens to compare by skin prick and nasal provocation testing as well as by serol. in vivo sensitivity with antibody-binding capacity in 24 pollen allergic

patients and eight control individuals. Results from biol. tests were correlated with each other and with allergen-specific IgE and IgG1-4 levels. IgE-reactive allergens induced immediate skin and nasal reactions, but the intensity of the allergic tissue reactions was not correlated with either the levels of allergen-specific IgE or the levels of allergen-specific IgG antibodies. Less frequently detected allergens with low IgE-binding capacity were able to induce strong allergic reactions comparable to those caused by major allergens with high IgE-binding capacity. In contrast, skin test and nasal provocation results were significantly correlated ($r = 0.63$, $p < 0.01$). Our study thus demonstrates on a mol. level that skin testing provides a better reflection of immediate type respiratory sensitivity than serol. measurements. These results have implications for allergy diagnosis and, in particular, for the selection of relevant allergen components for specific immunotherapy.

L17 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2001:370418 Document No. 135:165643 Nuclear magnetic resonance studies of allergens. Rosch, P. (Department of Biopolymers, University of Bayreuth, Bayreuth, 95440, Germany). Journal of Chromatography, B: Biomedical Sciences and Applications, 756(1-2), 165-177 (English) 2001. CODEN: JCBBEP. ISSN: 0378-4347. Publisher: Elsevier Science B.V..
AB A review with 55 refs. Topics discussed include solution structures of ragweed allergens Amb a5 and Amb t 5; dust mite allergens Der f2 and Der p2; timothy grass allergen **Phl p2**; birch allergen Bet v I; and cherry allergen Pru av 1.

L17 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
2000:163611 Document No. 133:162982 Phleum pratense-specific T cells of allergic rhinitis patients display a broader recognition pattern than Phleum pratense-specific serum immunoglobulin E. Van Neerven, R. J. J.; Arnved, J.; Ipsen, H. (ALK-Abello, Horsholm, Den.). Clinical and Experimental Allergy, 30(2), 242-254 (English) 2000. CODEN: CLEAEN. ISSN: 0954-7894. Publisher: Blackwell Science Ltd..
AB The role of allergen-specific CD4+ T lymphocytes in the pathophysiol. of atopic disease is well established. Previous studies on allergen-specific T-cell responses have focused on the recognition of single major allergens to identify T-cell epitopes. However, it is not clear whether immune responses to allergen exts. are exclusively targeted at major allergens or whether addnl. proteins are recognized. Here the authors describe the P. pratense-specific IgE and T-cell responses of 6 allergic rhinitis patients. Reactivity was measured to size-separated fractions of a P. pratense extract as well as to the purified major allergens Phl p 1, Phl p 2/3, and Phl p 5. The specificity of the patients' serum IgE, measured in a fluid phase assay, was restricted to 1 or 2 of the major allergens. Even though the majority of the patients had IgE antibodies reactive with a single major allergen, one patient reacted with both Phl p 5 and with Phl p 2/3. Anal. of the T-cell repertoire with P. pratense-specific T-cell lines (TCLs) and CD4+ T-cell clones (TCCs) revealed that at least 6 different proteins were recognized, including the 3 major allergens, most notably Phl p 5. Simultaneous production of IL-5 and interferon (IFN)-γ was detected in supernatants of the TCLs stimulated with P. pratense extract and the major allergens. Thus, allergic rhinitis patients have a large pool of circulating allergen-specific CD4+ T cells that recognize many different proteins in an allergenic extract, whereas only a small number of these proteins are recognized by serum IgE.

L17 ANSWER 5 OF 6 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 1
1997:243758 Document No.: PREV199799542961. X-ray crystal structures of birch pollen profilin and **Phl p2**. Fedorov, Alexander A.; Ball, Tanja; Valenta, Rudolf; Almo, Steven C. [Reprint author]. Dep. Biochemistry, Albert Einstein Coll. Med., 1300 Morris Park Ave., Bronx, NY 10461, USA. International Archives of Allergy and Immunology, (1997) Vol. 113, No. 1-3, pp. 109-113.

CODEN: IAAIEG. ISSN: 1018-2438. Language: English.

AB Background: Type 1 allergy affects 20% of industrialized populations and thus represents a major health care issue. The symptoms of type 1 allergy, which include rhinitis, conjunctivitis, dermatitis and asthma, are elicited by the crosslinking of IgE receptors through polyvalent allergens. A detailed understanding of the cell surface phenomena and the rational development of new therapies require high-resolution structural information. Methods: The structures of two widespread allergens, birch pollen profilin (BPP) and **Phl p2** have been solved by multiple isomorphous replacement. Refinements are underway to 2.4 and 2.0 ANG , respectively. In addition, the IgE-reactive epitopes of BPP where identified by screening an epitope expression library with the serum IgE of an allergic individual. Results: BPP exhibits an alpha/beta-fold which is similar to the mammalian and amoeba profilins. The structure of **Phl p2** is a compact eight-stranded beta-barrel.
Screening an epitope library of BPP identified three major epitopic regions involved in IgE binding, including the amino and carboxy-terminal alpha-helices. These regions also interact with the physiologically relevant ligands of profilin, actin and proline-rich peptides.
Conclusions: The distribution of IgE-binding sites on BPP allows for the productive interaction with IgE antibodies of different epitope specificities required for efficient signal transduction. These epitopes correspond to the most highly conserved regions of the profilin molecule and thus provide the molecular basis for allergen cross-sensitivity. Due to steric considerations, the involvement of these epitopic regions in the binding of physiologically relevant profilin ligands indicates that the native profilin is the species responsible for eliciting the allergic response. A comparison of the BPP and **Phl p2** structures shows that there is no preference for secondary structural elements in the allergic response. The detailed chemical and physical description of the major reactive epitopes provides a data base for the design of tight-binding monovalent ligands which can prevent receptor aggregation and thereby reduce the allergic response.

L17 ANSWER 6 OF 6 MEDLINE on STN DUPLICATE 2

96213652 Document Number: 96213652. PubMed ID: 8613635. Immunologic characterization of purified recombinant timothy grass pollen (Phleum pratense) allergens (Phl p 1, **Phl p2**, Phl p 5). Vrtala S; Susani M; Sperr W R; Valent P; Laffer S; Dolecek C; Kraft D; Valenta R. (Institute of General and Experimental Pathology, University of Vienna, Austria.) JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1996 Mar) 97 (3) 781-7. Journal code: 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB BACKGROUND: Grass pollen allergens belong to the potent elicitors of type I allergy. Approximately 40% of allergic individuals display IgE reactivity with grass pollen allergens. In previous studies we have reported the complementary DNA cloning and expression in Escherichia coli of three of the most relevant timothy grass pollen allergens: Phl p 1, Phl p 2, and Phl p 5. OBJECTIVE: To achieve high level expression of immunologically active timothy grass pollen allergens in E. coli, the cDNAs were inserted into expression plasmids. METHODS: The three recombinant grass pollen allergens were expressed at high levels in E. coli as recombinant nonfusion proteins, purified by conventional protein chemical methods and tested for their IgE-binding capacity by immunoblot and ELISA, as well as in histamine release assays. RESULTS: Milligram amounts of pure recombinant allergens were obtained from cultured E. coli. IgE binding to purified recombinant Phl p 1, Phl p 2, and Phl p 5 could be demonstrated by immunoblot and ELISA. With ELISAs the percentage of grass pollen-specific IgE directed against the individual recombinant allergens could be estimated. In addition, the purified recombinant timothy grass pollen allergens induced dose-dependent and specific histamine release from patients' blood basophils. CONCLUSION: Purified recombinant timothy grass pollen allergens represent useful tools for diagnosis and therapy of grass pollen allergy.